Guidance for Industry

Preparing Data for Electronic Submission in ANDAs

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
OGD
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I. INTRODUCTION

This guidance is intended to provide assistance to applicants submitting data in electronic format to the Office of Generic Drugs (OGD) in abbreviated new drug applications (ANDAs). This guidance should be used in conjunction with the entry and validation application (EVA) user's manual, available on OGD's electronic submission web site. The web site is currently maintained by the University of Maryland, Baltimore County (UMBC), under a contract with the FDA's Office of Pharmaceutical Science (OPS). The web site address is: http://mundos.ifsm.umbc.edu/fda_eva. This guidance contains a glossary of the terms related to submitting ANDA data in electronic format.

II. BACKGROUND

In the *Federal Register* of March 20, 1997 (62 FR 13430), the FDA published the Electronic Signatures Regulation (21 CFR Part 11). This regulation provides for the voluntary submission of parts or all of regulatory records in electronic format without an accompanying paper copy when we indicate in Docket 92S-0251 that we are ready to receive the electronic records.

The Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research have published two guidances for industry on submitting applications in electronic format, *Providing Regulatory Submissions in Electronic Format—General Considerations* (January 1999) and *Providing Regulatory Submissions in Electronic Format—NDAs* (January 1999). In the *General Considerations* guidance the Agency explains that a series of guidances are planned addressing additional regulatory submissions including ANDAs. An essential objective delineated in the January 1999 guidances is that an electronic submission should meet regulatory requirements, should be easily archived, and should be reviewable within specified time frames using FDA desktop equipment and programs.

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[1] This guidance has been prepared by the Office of Generic Drugs (OGD), Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA). This guidance document represents the Agency's current thinking on the submission of electronic data for (ANDAs). It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

On June 1, 1998, the President instructed all Federal agencies to ensure the use of plain language in all new documents. This guidance reflects Agency efforts to comply with the President's plain language initiative.

At this time, OGD does not have archiving capability and has not yet prepared a guidance for the planned series to address ANDAs. When OGD is prepared to archive electronic ANDAs, a guidance will be developed consistent with the Agency's good guidance practices policy (62 FR 8961, February 27, 1997). At that time, information from this guidance will be incorporated into the Agency guidance on electronic regulatory submissions.

Pending completion of a guidance on submitting an ANDA in electronic format and in the absence of archiving capability, you must still submit a complete paper ANDA, organized according to the requirements in 21 CFR 314.94. OGD currently has a process that allows the submission of some types of data and certain text information in electronic format in addition to the paper submission. That process is the subject of this guidance.

Being able to submit and receive information in electronic format in an ANDA is expected to yield many benefits to industry and FDA, including a more consistent submission, a more consistent and rapid review, and a reduction in archiving and storage space. An additional objective is to establish a structured database of technical information associated with generic drug applications.[2] The database would serve as a valuable Agency resource, improving Agency review staff's access to information about formulation, manufacturing, bioequivalence, and other data, thus improving the efficiency, quality, and consistency of generic drug product reviews.

III. WHAT IS THE STRUCTURE OF ELECTRONIC FILES ASSOCIATED WITH AN ANDA?

Electronic submissions of information in an ANDA should be separated into parts to address (1) bioequivalence information and (2) chemistry, manufacturing, and controls (CMC) information. At this time, an applicant may choose to submit either or both parts electronically. Each part should consist of a defined set of three electronic files: (1) an electronic submission document (ESD), (2) a set of data files and (3) a companion document. The templates for all three of these file types can be found on the project web site (data files are planned for the CMC but are not now available).

A key element to entering information for an electronic ANDA submission is the entry and validation application (EVA). EVA is a Windows-based data entry program. It is a user friendly, automated tool developed to facilitate the creation of the standardized format required for the ESD for an ANDA submission. Although ANDA applicants may create the ESD without using EVA, this is not recommended because EVA eliminates the need for expert computer and database knowledge. Users should have a thorough understanding of the structure of the ESD before attempting alternative solutions. This can be achieved by consulting the documentation available on the EVA web site.

[2] This database was developed under a contract between FDA and the University of Maryland at Baltimore County.

A. What Is The Electronic Submission Document – ESD?

The ESD is a simple text document, developed by the FDA, that is coded for automated processing using special characters and symbols. It consists of sections and subsections that define relevant portions of the ANDA. The ESD is formatted to facilitate loading data into OGD's database and subsequently into the reviewer tools. The markup provides tags that tell the computer how to sort the information as it is uploaded into the OGD database. The markup used in the ESD is visible as a series of letters and characters such as slashes and colons. For example the tag indicating ANDA number is ::ANDA_NO::. The use of the ESD eliminates the need for OGD staff to retype submitted data into OGD's database.

B. What Are the Data Files?

The data files provide standard formats for the sponsor to present various types of data that should be submitted to complete the review. The data files subsequently become part of OGD's Excel program/review tool, which is used by OGD review staff to help facilitate the review. In addition, these data files can be analyzed using SAS or other statistical packages. For a complete list of the types of data files that are currently defined, see the EVA user manual on the project web site. As stated earlier, data files have not yet been defined for the CMC part of the electronic ANDA submission.

C. What Is the purpose of the Companion Document?

The companion document is a word-processed report in an electronic format that contains narrative explanations to supplement the information provided in the ESD.[3] The document provides a place where additional textual information and explanations can be provided to the reviewer. Standard templates have been developed for these documents. The templates provide suggestions about the content of the companion document. Because submissions may vary somewhat in content, the templates have been developed to allow flexibility in informational content. If any applicant determines that a portion of the suggested companion document does not apply to their submission, this section may be left out. In addition, applicants may add sections at the end of the companion document.

The companion document templates may be obtained from the project web site. Applicants can download these templates and paste information directly into them from other sources.[4] Applicants can also create companion documents by typing the correct section headers into an existing document. For successful use, spacing, case and

[3] Although OGD can accept documents produced with most of the common word processing software, the preferred format is MSWORD 97.

[4] Nothing in the templates constitutes a change to or revision of any other written guidance, policy, or position taken by OGD or the Agency as a whole, and nothing should be interpreted to make such a change. If you have a question about a template, please contact the OGD Electronic Submissions Coordinator at 301-827-5845.

punctuation should exactly match what is presented in the template. The most common errors include omitting periods, using all upper case letters, and adding extra spaces or characters.

IV. HOW DO I GET STARTED?

A. Registration

To develop an electronic ANDA submission using the ESD, you should obtain a unique three-character identification by registering through the project web site. Others who are interested in EVA (such as CROs) can also register. All registered users are kept informed of significant events via electronic mail. Significant events include new version releases, changes to file formats, and issuance of user advisories.

B. Is There a Standard Operating Procedure (SOP) for the Program?

The SOPs for both the CMC and bioequivalence portions of the program are available on the project web site. You should review these SOPs as well as the other documentation available before beginning an electronic ANDA submission.

V. WHAT TYPES OF APPLICATIONS CAN I SUBMIT WITH THIS SYSTEM?

OGD believes that the CMC portion of this system can accommodate all types of ANDAs. The bioequivalence portion has certain limitations with respect to the types of drug products that can be accommodated. It primarily supports the preparation of electronic data associated with ANDAs for oral dosage forms. Other dosage forms can be accommodated where bioequivalence is established through the measurement of blood or plasma concentrations (e.g., transdermal dosage forms). With respect to bioequivalence studies, EVA will accommodate standard cross-over as well as replicate cross-over study designs. For a complete list of the dosage forms that are supported, see Appendix B. You should contact OGD before attempting to use the system for any dosage form not listed in Appendix B.

VI. WHAT IS THE ENTRY AND VALIDATION APPLICATION – EVA?

The EVA software organizes the structure of the ESD and presents it to the applicant as a series of data entry forms. Once these forms are completed, the ESD can be exported from EVA for submission to OGD by clicking a button.

A. How Do I Obtain the EVA Software?

The EVA program is available free of charge by downloading at the project web site (http://mundos.ifsm.umbc.edu/fda_eva). Enter the Internet site and go to the download software section. There you will find instructions for downloading and installing the

software onto your PC. Because the installation instructions may change from time to time due to advancing knowledge, they should be reviewed before each download.

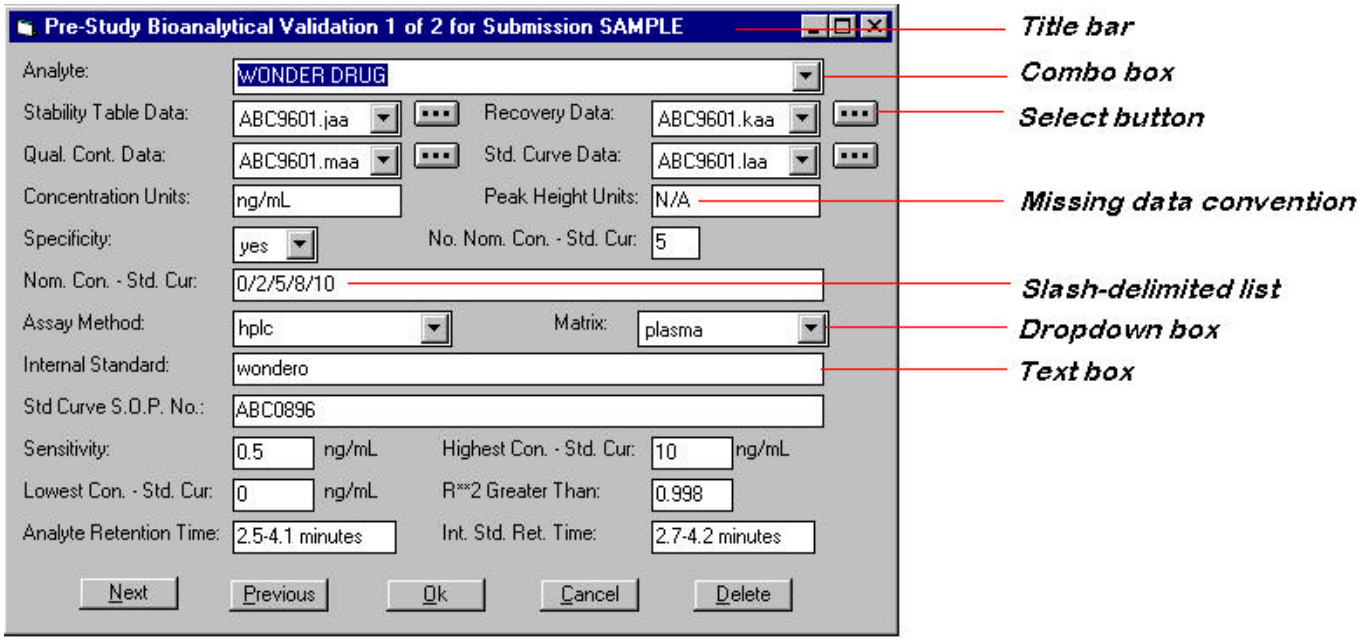
EVA is available with or without sample data. The sample data version of EVA provides a sample submission already loaded into the program. The sample submission provides an added level of assistance to novice users. Where a question arises about the type of information that should be entered on an EVA form, the applicant can open the sample submission to examine a completed form. A more experienced EVA user may find it unnecessary to refer to the sample data.

B. How Is Data Entered in EVA?

The EVA program provides a series of data entry forms (Fig. 1). Forms are accessed through hierarchy charts (Fig. 2) that are presented in either the bioequivalence or CMC view of the EVA window. This hierarchy chart lists each form according to the corresponding data structure in the ESD. The hierarchy chart displays the organizational structure of EVA information according to the subordinate rank of the information. For example, the data entry forms are subordinate to the *submission info* form. The EVA hierarchy chart is a list of forms in the workspace of the main EVA window.

You can select a form for data entry and/or editing by double clicking on the hierarchy chart folder for the form of interest. In addition to using the hierarchy chart, some forms contain tabs for moving down the hierarchy to enter additional data on the same subject.

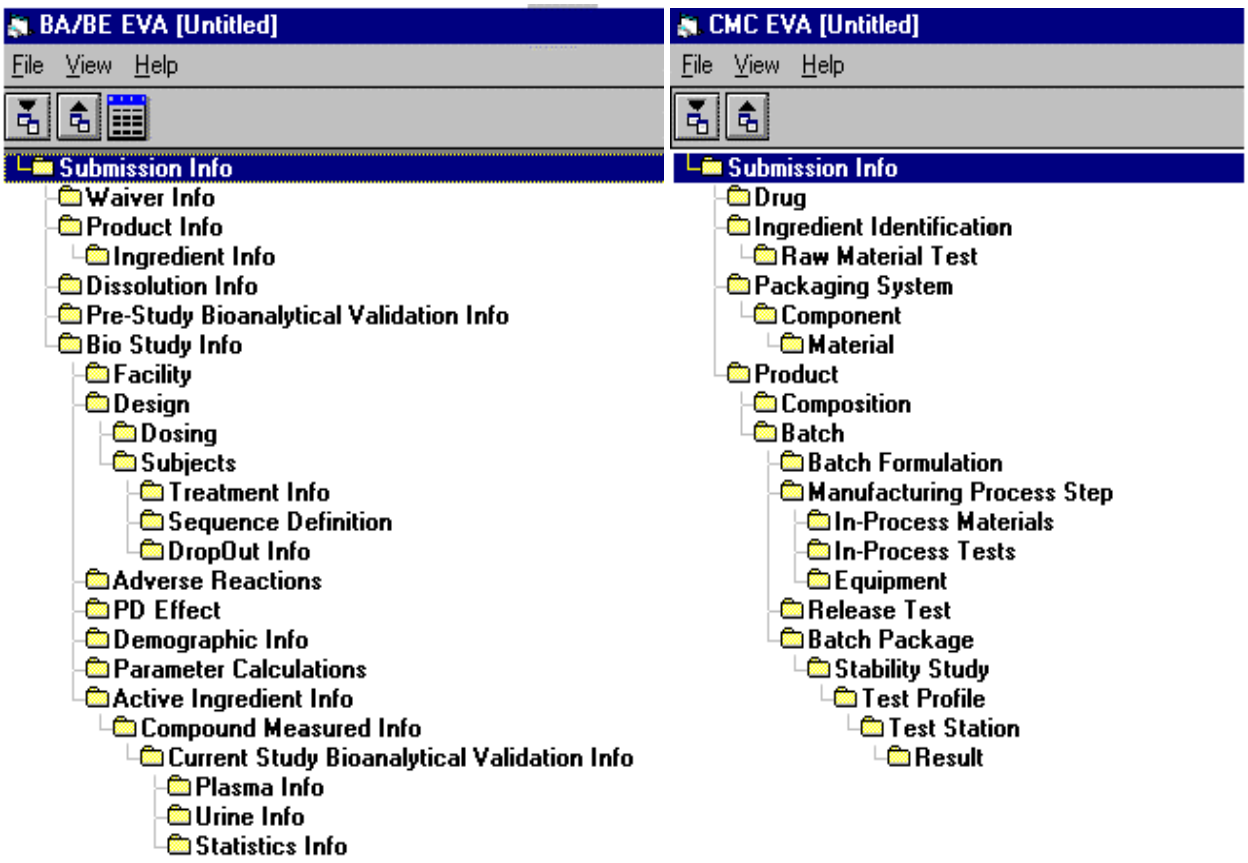
FIGURE 1: A TYPICAL EVA FORM



A detailed description of each form is available from the on-line help feature and in the EVA user manual. An additional source of information about the forms is the *context sensitive* or *micro* help. When the mouse pointer is placed over one of the data entry areas, a description of the information that should be typed in this area appears on the status bar. The status bar is the extreme lower border of the EVA window. The *context sensitive* help is available for most of the EVA data entry areas. Areas of a form also can be clicked to display the context sensitive help.

Because each EVA form corresponds to a section of the ESD, some applications call for the use of multiple copies of the same form type within a single submission. This is true whenever a submission includes multiple pieces of information of the same type. For example, for items such as ingredients on the bioequivalence portion and batches on the CMC portion, multiple copies of the same form type may be called for.

FIGURE 2: EVA HIERARCHY CHARTS



C. What Do I Do About Missing Data?

As part of the validation built into EVA, the program will not save a form if any of the boxes on the form are left blank. There are times when the data for a particular box are unavailable, or the box simply does not apply to the current submission. Sometimes the information is too complex to fit into the space provided in the box. In such cases, you can enter N/A into the box. The N/A will not appear in the database itself, but is used to indicate that this data element was intentionally left out of the ESD. A similar situation may occur when creating data files. Sometimes a particular data point may not be available. In this case, you can use a dot or period (.) where the missing data point belongs.

D. How Do I Produce the ESD?

Once all the forms relevant to the submission are completed, the *export feature* of EVA can be used to produce the ESD. Click on the word *file* on the menu bar and a menu appears. Place the mouse pointer on the words e*xport to ESD* and click. A form containing two boxes will appear. An icon on the tool bar will accomplish the same thing with a single mouse click. The export icon appears as two rectangles under an arrowhead pointing up.

The *submission ID* box displays the submission that will be exported. The *directory path* box displays the location where the ESD will be stored. A *selection* button next to the *directory path* box allows the applicant to select the location where the ESD will be stored. This location is at the discretion of the sponsor.

Once *submission for export* and the location for the ESD are selected, clicking on the *OK* button will produce the ESD and store it at the selected location. When the export is completed, a message appears on the screen. This message will indicate whether or not the export procedure was successful in producing a valid ESD. The message will provide the name and the location of the ESD file and two other files, the *user verification* and *EVA log* files. The *user verification* file contains the same information as the ESD except that it is converted to a style that is easier to read than the ESD. This file is intended to simplify the quality control process for the ESD.

The *EVA log* file lists the date and time of export, the version of EVA that was used, the name of the submission as it appears in EVA, and the export file name and its location. This file also contains a list of all the errors that might have occurred during the export procedure. Any errors listed should be corrected and a new export performed before submitting the ESD.

The ESD and the *EVA log* files are submitted as part of the electronic submission. The *user verification* file is for use by the applicant and need not be submitted.

E. How Can I Get an ESD into EVA?

Sometimes applicants find it helpful to bring the information from an ESD into the EVA program. One occasion where this occurs is when a CRO prepares an ESD and the applicant needs to add some additional information.

A previously exported ESD can be entered into EVA using the *import* feature. Click on the word *file* on the menu bar and a list appears. Place the mouse pointer on the words *import from ESD* and click. A form appears with a single *source file name* box. There is an icon similar to the one for export that will accomplish the same thing with a single click. The import icon appears as two rectangles under an arrowhead pointing down.

The file name and location of the ESD are entered into the source file name box by typing or use of the *selection* button. The *selection* button next to the source file name box allows the applicant to browse the computer for the location of the ESD. Once the ESD file is located, double click on it, and the file name and location will appear in the source file name box. Click on the *OK* button and the import procedure will begin.

When the import is completed, a message will appear on the screen. The title bar on the message will indicate whether or not the import was successful. The message gives the location of the EVA log file, which will list any errors that may have occurred.

VII. HOW SHOULD I PREPARE THE ESD, DATA FILES, AND COMPANION DOCUMENT FOR SUBMISSION TO OGD?

The completed ESD, data files, and companion document should be copied to either a 3½" diskette or CD for submission to OGD. If the size of your files requires additional space, you can use a second diskette. If you need three or more diskettes, you may have included more information than is necessary in your companion document.

The diskettes should be clearly labeled with the following information:

ESD Electronic Submission xxx
(Where xxx = either CMC or BIO as appropriate)
Company Name
Drug Product Name and Strength
ANDA Number (if available)
Whether it is the ESD, the Companion Document, or both
Submission Date and Type (i.e., original, amendment)
Name and Phone Number of Contact Person
(The contact person should have knowledge of and access to the electronic submission.)

The diskettes should be placed in a protective envelope or bubble wrap.

A. How Do I Notify OGD that a Submission Includes Electronic Files?

When receiving an ANDA with electronic information, OGD should be immediately aware that an application includes electronic files so that the ESD, data files and companion document can be processed prior to review. An easily identified statement should be typed on the front page of the application cover letter to indicate this information.

Please include the following statement on the cover letter of each ANDA that is associated with an ESD.

> *This application includes a CMC and/or bioequivalence ESD electronic submission. The diskettes (or CD) are enclosed.*

B. What If I Cannot Send the Electronic Files When I Send the Hard Copy?

The electronic files should be submitted at the same time as the hard copy of the submission. However, to encourage participation in the ANDA electronic submission project, OGD is providing 30 days for the submission of the electronic files after submission of the paper copy. Once the review of the hard copy application has begun, we will not interrupt or delay it to accommodate late arriving or unusable electronic files. As a result, electronic files submitted after the 30-day period may not be used during the review.

A hard copy application that is submitted before the electronic files should contain a notification on the front page of the cover letter. The following statement is recommended:

> *This application will include a CMC and/or bioequivalence ESD electronic submission. The diskettes will be sent as new correspondence within 30 days.*

When submitting the electronic files separately, always include a copy of the original application cover letter.

C. Declaration

Applicants should provide a written declaration (with an original signature) that the information in the electronic files (ESD, data files, and companion document) is identical to the information provided in the paper (hard copy) submission. The data entered into EVA should be a portion of information that is within the hard copy. No differences should exist between information in the electronic submission and in the hard copy, although data presentation may be different. The following statement can be used for the written declaration:

The information contained in the electronic submission (reference the submission by date and drug product) is not different from the information contained in the hard copy submission (reference the submission by date and drug product).

If the electronic submission follows the paper submission, the declaration should be included with the electronic submission.

D. Where Do I Send Electronic Files for Review by OGD?

At this time, electronic files should be sent to the same address as the paper submissions.

Mail:
Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855

Courier or parcel service:

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

VIII. BIOEQUIVALENCE

This section contains information that will help in the preparation of the electronic files for the bioequivalence portion of ANDAs. At this time, there are three types of electronic files associated with the bioequivalence portion of an ANDA: (1) the ESD, (2) the data files, and (3) the companion document.

A. Notes On Bioequivalence Data Entry In Eva

1. What do I do if a contract research organization (CRO) conducts the bioequivalence studies?

Experience indicates that most of the EVA bioequivalence data entry is performed by CROs on behalf of ANDA applicants. This does not relieve the applicant of the responsibility of ensuring that the data entered into EVA are complete. Based on the electronic ANDAs received to date, there are three sections in EVA that are generally not completed by the CRO. They include waiver information, ingredient information, and dissolution information. The applicant should add this information before sending the electronic ANDA to the Agency.

2. What is the purpose of the ID fields on the product info and treatment info forms?

EVA uses these IDs to track your elements and their interrelationships. You can pick an ID of your choosing for each of these fields. To help avoid confusion on the part of the reviewer, you should select meaningful designations for these fields. For example, for treatment ID, instead of IDs like *A* and *B*, *FED* and *FAST* may be more appropriate. This will help the reviewer to easily identify which treatment is associated with the data he or she is viewing.

3. How are adverse events reported electronically?

OGD is in the process of changing the way adverse events can be submitted electronically. At this time, users have the option of entering the data in EVA (the original method) or creating a data file outside of EVA (the new method). The format for the data file can be found on the project web site. You should use the data file method because planned modifications to EVA will eliminate the first option.

4. Must I enter pharmacodynamic (PD) effects if I use EVA?

To provide a flexible data entry program for the preparation of electronic bioequivalence files, some forms that do not apply to all ANDAs are included in EVA. One such form is the PD (pharmacodynamic) effect form. This form is available if your submission includes PD effect data. However, the presence of this form does not mean that you should report PD effect data when you would not otherwise include such data. Nothing in EVA should be viewed as a requirement for an ANDA.

5. Why is the term lbm (pounds mass) used on the demographic info form?

One of the choices for weight units on the demographic info form has caused some confusion for some EVA users. The choice is *lbm*, which stands for *pounds mass*. This should be selected when weight is measured in pounds. It is used for

compatibility with Microsoft Excel, which was used as the basis for the bioequivalence electronic reviewer tool.

6. *Must I include an additional bioequivalence diskette with the 3 Plasma Concentration, Plasma Pharmacokinetic parameters, and KEL Estimation files if I'm generating the electronic submission per this guidance?*

No, you do not need to include the 3 above files on a separate diskette. The 3 files are included in the set of files needed to complete the electronic submission.

B. What Kinds of Information Should I Put in a Bioequivalence Companion Document?

The OGD Division of Bioequivalence developed the outline chosen for the bioequivalence companion document. The purpose of the bioequivalence companion document is to assist in the efficiency and quality of electronic reviews. It is expected that this document will continue to evolve as the program expands. A copy of the current bioequivalence companion document template can be obtained from the project web site.

The bioequivalence companion document should consist of both narrative text for supporting information that is not easily included in the ESD through EVA and a series of tables. These tables have been well defined by the Division of Bioequivalence and are described completely in the template. The bioequivalence companion document should be a concise summary of study design and findings. Excessive use of graphics and large tables that do not fit within the template's margins is discouraged because they make the document cumbersome to review. Chromatograms, case report forms, SOPs, SAS output, and similar documentation should not be scanned into the companion document. Reference to the hard copy should be used for these types of information.

IX. CMC

This section contains some information that will help in the preparation of the electronic files for the CMC portion of ANDAs. At this time, there are only two electronic files associated with the CMC portion of an ANDA submission: an ESD and a companion document. It is probable that data files will be added to the CMC electronic file formats in the future.

A. Special Strategies for CMC Data Entry In EVA

1. *Ingredient information*

Ingredient information will normally be entered into EVA for each batch for each strength. The forms for this information are high on the hierarchy chart so that this information does not need to be retyped each time it is called for. Plan ahead and enter this information first so that it is easily accessible when called for.

The ingredient information form is used for both active and inactive ingredients. The form should be completely filled out for each lot of active ingredient that is used in the ANDA. For inactive ingredients, it is best not to use the lot number information columns. For inactive ingredients, provide information pertaining to the acceptance specifications for each inactive ingredient and enter N/A for the lot number. For inactive ingredients, provide testing information to describe the test specifications, but not test results data (N/A is entered for laboratory, date, and result boxes).

It is common for applications to refer to USP/NF monograph specifications. This is possible in EVA as well. When reference to the entire USP monograph is desired, the parameter box should list all sections (e.g., assay, identity, chloride). The *method* and *specifications* boxes should reference the USP monograph. The *comments* box should explain that this single test form refers to multiple test specifications.

2. Packaging system

The packaging system form is much like the ingredient information form in that the information is lower in the hierarchy chart on the batch package form. It is advantageous to completely fill out all three tabs of the packaging system form to streamline data entry lower on the hierarchy chart.

Where applicable, you can refer to the USP/NF monograph specifications on the material specifications form.

3. Batch information

The batch form provides two tabs, one for the general description and one for the formulation of one batch for one product in the application. Additional batches can be described by using the *new* button to obtain an additional blank form.

The manufacturing process step form provides four tabs for the description of a single manufacturing step. These tabs are not intended to provide for exact duplication of the batch records. They provide for a reasonable description of the manufacturing process.

Note: If a particular tab on this form requires no entries, do not enter a record that contains all N/A. Leave the tab blank.

The *Step #* box needs to be filled with a whole number. Decimals or dashes should not be used.

Many applicants use a manufacturing procedure sometimes referred to as common granulations. EVA will accommodate this by including a description of the common granulation on the ingredient information form. This common

granulation's ingredient ID can then be used on the in-process materials form. Testing specifications applicable to the common granulation should be entered on the in-process tests form.

4. Stability information

The stability study form is available for each batch described in EVA. This form has four tabs to describe one stability study relevant to a batch. The *New* button should be used to access additional blank forms for each additional stability study relevant to a batch.

For blank batch descriptions, the stability forms should describe the proposed stability studies for manufacturing batches that are the subject of stability studies. For executed batches, the stability forms should describe the stability testing that was done on these batches in support of the ANDA.

The test station and individual results tabs provide for entry of stability test data. The test station tab is for entry of test data including averaged dissolution data. The individual results tab provides a place for entry of individual sample data from dissolution tests. These two tabs are optional and can be left blank. There is no need to enter N/A into any of the boxes. This information should still be provided in the hard copy and may be included in the companion document.

B. What Kinds of Information Should I Put in a CMC Companion Document?

The companion document should be mostly narrative text for supporting information that is not easily included in the ESD through EVA. Some tables and graphics can be included when they are kept within the text margins. Excessive use of graphics and large tables cause the document to be cumbersome to navigate during review. For example, reference to the hard copy should be provided for the FDA Form 356H, signed certifications, chromatograms, spectra, and batch records. These documents should not be scanned into the companion document. The CMC Companion Document template is in outline format and can be obtained from the project web site.

X. WHAT IF I HAVE A QUESTION?

Please contact our technical support personnel through the project web site. In addition, you can direct questions to the OGD Electronic Submissions Coordinator at 301-827-5845.

GLOSSARY

This glossary contains brief descriptions of some of the terms associated with electronic submission of ANDAs. Additional information on these and other electronic submission terms may be obtained from the EVA User Manual, EVA on-line help, or the project web site.

Blank Batch: A blank batch is a description of the full-scale production batch described in the ANDA. This section of EVA is to record a description of the batch.

Box: A box is a rectangular area where data can be entered on a form. For example, the *submission info* form has a box where the submission ID is entered.

Button: A button is a graphical representation of a Computer command. Clicking on a button causes some action to take place. For example the *OK* button in EVA saves the information on the current form to EVA and returns the applicant to the hierarchy chart.

Context Sensitive Help: Context sensitive help provides information on the status bar about a box, button, or list box on the current form. In EVA this help is in the form of micro-help displayed in the status bar.

ESD (Electronic Submission Document): A simple text document that is coded for automated processing with a strict markup consisting of special characters and symbols. It comprises sections and subsections that define the generic drug product application to be reviewed by the Agency.

EVA (Entry and Validation Application): EVA is a Windows-based, data entry program that creates ESD files. It is a user friendly, automated tool developed to facilitate the creation of the standardized format required for electronic ANDA submissions.

Executed Batch: The executed batches are descriptions of the batches that were manufactured to support the approval of the ANDA. An executed batch may or may not be a full-scale production batch.

Folder: A folder is where documents and programs are stored. In previous versions of Windows, folders were called directories.

Form: A form is a window into which information is entered.

Hierarchy Chart: The hierarchy chart displays the organizational structure of EVA information according to the subordinate rank of the information. For example, all the data entry forms are subordinate to the submission form. The EVA hierarchy chart is a list of forms in the workspace of the main EVA window.

List Box: A list box is a box in which a list of selectable values is displayed. You can distinguish a list box by the underlined down arrow icon to the right of the box. To view the list of the selectable values, click on the icon. To select a value, click on it and the value will be placed in the box. There are two types of list boxes used in EVA, the editable and noneditable list boxes.

Non editable list box means you can only select from the values displayed in the list. The down arrow being attached to the box distinguishes a non editable list box.

The second type of list box is an editable list box, which means you can either select from the values displayed in the list or enter your own. An editable list box is distinguished by the down arrow being separate (just to the right) from the box.

Log File: A log file contains information regarding the version of EVA that was used, the submission name, date, and other information. It also contains a statement regarding whether or not the operation was successful. If there are errors with the import or export, they will be listed in the log file.

Markup: A markup is a method to provide the document with computer readable tags. These tags tell the computer how to sort the information as it is uploaded into the database.

Path: The path is the fully specified directory (folder) name where files are stored on a computer.

Status Bar: The status bar is located at the bottom of the main EVA window and displays helpful information about the current form. For example, the status bar displays context sensitive help for all forms.

Submission: The term submission within EVA refers to all the information for a single ESD export. EVA tracks this information with a submission ID that allows for editing and exporting the submission.

Title Bar: The title bar is the upper border of a window. It is large enough to contain limited information about the window.

The EVA title bar displays the active view and the submission that are currently selected. If no submission is currently selected for editing, *untitled* is displayed on the title bar. Each form displays information in the title bar for the window corresponding to each form.

Tool Bar: The EVA tool bar is just below the title bar. The tool bar contains three buttons that allow access to the *import*, *export* and the *data file editor* options. These options are also available on the menu bar.

URL (Uniform Resource Locator): A standard for specifying the location or address of a file on the Internet. These addresses generally start with a protocol name followed by specific information that identifies the computer where the page of interest is stored.

Windows: This refers to any of the series of user-interface/operating systems created by Microsoft. These systems are known as Windows 3.x, Windows 95, Windows 98, and Windows NT.

Workspace: The workspace is the area between the tool bar and the status bar. The boxes used for EVA data entry are contained in the workspace.

APPENDIX A: DOSAGE FORMS ACCOMMODATED BY EVA

Dosage Form	CMC	Bioequivalence
AEROSOL, METERED	**ACCOMMODATED**	**NOT** [5]
BAR, CHEWABLE	**ACCOMMODATED**	**ACCOMMODATED**
CAPSULE	**ACCOMMODATED**	**ACCOMMODATED**
CAPSULE, COATED PELLETS	**ACCOMMODATED**	**ACCOMMODATED**
CAPSULE, DELAYED RELEASE PELLETS	**ACCOMMODATED**	**ACCOMMODATED**
CAPSULE, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
CONCENTRATE	**ACCOMMODATED**	**NOT APPLICABLE**
CREAM	**ACCOMMODATED**	**ACCOMMODATED**
CREAM, AUGMENTED	**ACCOMMODATED**	**ACCOMMODATED**
CREAM, SUPPOSITORY	**ACCOMMODATED**	**ACCOMMODATED**
DISC	**ACCOMMODATED**	**NOT APPLICABLE**
DRESSING	**ACCOMMODATED**	**NOT APPLICABLE**
DRUG DELIVERY SYSTEM	**ACCOMMODATED**	**ACCOMMODATED**
ELIXIR	**ACCOMMODATED**	**ACCOMMODATED**
EMULSION	**ACCOMMODATED**	**NOT**
ENEMA	**ACCOMMODATED**	**ACCOMMODATED**
FIBER, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
FILM, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
GAS	**ACCOMMODATED**	**NOT APPLICABLE**
GEL	**ACCOMMODATED**	**ACCOMMODATED**
GRANULE	**ACCOMMODATED**	**ACCOMMODATED**
GRANULE, DELAYED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
GRANULE, EFFERVESCENT	**ACCOMMODATED**	**ACCOMMODATED**
GRANULE, FOR RECONSTITION	**ACCOMMODATED**	**ACCOMMODATED**
GRANULE, FOR RECONSTITUTION, EX. REL.	**ACCOMMODATED**	**ACCOMMODATED**
GUM, CHEWING	**ACCOMMODATED**	**ACCOMMODATED**
IMPLANT	**ACCOMMODATED**	**ACCOMMODATED**
INHALANT	**ACCOMMODATED**	**ACCOMMODATED**
INJECTABLE	**ACCOMMODATED**	**ACCOMMODATED**
INJECTABLE, LIPID COMPLEX	**ACCOMMODATED**	**ACCOMMODATED**
INJECTABLE, LIPOSOMAL	**ACCOMMODATED**	**ACCOMMODATED**
INSERT	**ACCOMMODATED**	**ACCOMMODATED**

[5] *NOT* means not accommodated.

INSERT, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
INTRAUTERINE DEVICE	**ACCOMMODATED**	**NOT APPLICABLE**
JELLY	**ACCOMMODATED**	**ACCOMMODATED**
LIQUID	**ACCOMMODATED**	**ACCOMMODATED**
LIQUID, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
LOTION	**ACCOMMODATED**	**ACCOMMODATED**
LOTION, AUGMENTED	**ACCOMMODATED**	**ACCOMMODATED**
LOTION/SHAMPOO	**ACCOMMODATED**	**NOT**
OIL	**ACCOMMODATED**	**ACCOMMODATED**
OINTMENT	**ACCOMMODATED**	**ACCOMMODATED**
OINTMENT, AUGMENTED	**ACCOMMODATED**	**ACCOMMODATED**
PASTE	**ACCOMMODATED**	**NOT**
PASTILLE	**ACCOMMODATED**	**ACCOMMODATED**
PELLET	**ACCOMMODATED**	**ACCOMMODATED**
POWDER	**ACCOMMODATED**	**NOT**
POWDER FOR RECONSTITUTION	**ACCOMMODATED**	**ACCOMMODATED**
SHAMPOO	**ACCOMMODATED**	**NOT**
SOAP	**ACCOMMODATED**	**NOT**
SOLUTION	**ACCOMMODATED**	**ACCOMMODATED**
SOLUTION FOR SLUSH	**ACCOMMODATED**	**ACCOMMODATED**
SOLUTION, GEL FORMING/DROPS	**ACCOMMODATED**	**ACCOMMODATED**
SOLUTION/DROPS	**ACCOMMODATED**	**ACCOMMODATED**
SPONGE	**ACCOMMODATED**	**NOT APPLICABLE**
SPRAY	**ACCOMMODATED**	**NOT**
SPRAY, METERED	**ACCOMMODATED**	**NOT**
SUPPOSITORY	**ACCOMMODATED**	**ACCOMMODATED**
SUSPENSION	**ACCOMMODATED**	**ACCOMMODATED**
SUSPENSION, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
SUSPENSION/DROPS	**ACCOMMODATED**	**ACCOMMODATED**
SWAB	**ACCOMMODATED**	**NOT APPLICABLE**
SYRUP	**ACCOMMODATED**	**ACCOMMODATED**
TABLET	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, CHEWABLE	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, COATED PARTICLES	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, DELAYED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, DISPERSIBLE	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, EFFERVESCENT	**ACCOMMODATED**	**ACCOMMODATED**

TABLET, EXTENDED RELEASE	**ACCOMMODATED**	**ACCOMMODATED**
TABLET, ORALLY DISINTEGRATING	**ACCOMMODATED**	**ACCOMMODATED**
TAMPON	**ACCOMMODATED**	**NOT APPLICABLE**
TAPE	**ACCOMMODATED**	**NOT APPLICABLE**
TINCTURE	**ACCOMMODATED**	**ACCOMMODATED**
TROCHE/LOZENGE	**ACCOMMODATED**	**ACCOMMODATED**